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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/647,882

08/25/2003

Johannes Bartholomaus

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EXAMINER

CHOI, FRANK I

ART UNIT

PAPER NUMBER

1616

MAIL DATE

DELIVERY MODE

12/23/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/647,882	Applicant(s) BARTHOLOMAUS ET AL.	
	Examiner FRANK I. CHOI	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 October 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 44-76 is/are pending in the application.
- 4a) Of the above claim(s) 54-76 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 44-53 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/23/2008 has been entered.

Election/Restrictions

The Applicant previously elected without traverse of Group I in the reply filed on 11/6/2006 and species (1RS, 2RS)-3-(3-dimethylamine-1-hydroxy-1,2-dimethylpropyl)phenol. Claims 1-5, 9-12, 40-43 were prosecuted, including the final rejection (4/23/2008), to the extent they read on the elected species. As such, the restriction requirement/election of species was final. After a restriction requirement is made final, the only option is to file a petition with the Director. However, since the Applicant had previously elected the same without traverse, the Applicant waives the right to petition the Director and cannot now traverse the restriction requirement and election of species. See 37 CFR § 1.144. As such, new claims 44-53 will be prosecuted to the extent they read on the elected invention with claims 54-76 withdrawn as directed to the non-elected invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 44-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dyrsting et al. (US Pat. 6,077,822) in view of WO 00/12067 and EP 0 693 475.

Dyrsting et al. disclose that it is common practice in the pharmaceutical industry to use salt forms of drugs, e.g. with physiologically acceptable organic or inorganic acids and bases such as hydrogen chloride and for drugs with amine groups it is feasible to use salts with organic or inorganic acids (Column 1, lines 15-25). It is disclosed that drugs salts with sugar acids, such as monosaccharides, exhibit increased uptake and controlled release properties and that insoluble or poorly soluble drug-sugar acid salts have to be found to have a drug release profile that is not dependent on pH in the gastrointestinal tract (Column 1, lines 35-55). It is disclosed that many alkaline drug compounds cause irritation of tissue or mucosa, may also have an unpleasant taste and accordingly they can be administered provided with a polymeric film coating to delay drug release but that is disclosed that such coatings however add to the cost and complexity of formulation (Column 1, lines 28-34).

WO 00/12067 disclose that saccharinate salts of non-alkaloid organic bases provide improved organoleptic properties (page 2).

EP 0 693 475 disclose a 1-phenyl-3-dimethylaminopropane analgesic compounds of formula I, such as (1RS,2RS)-3-(3-dimethylamino-1-hydroxy-1,2-dimethylpropyl)phenol that can be converted in a known manner to their salts (Pages 5,15; See English language version - US Pat. 6,344,558, Column 5, lines 25-36, Column 15, lines 40-68).

Dyrsting et al. discloses the formation of drug salts with sugars. The difference between Dyrsting et al. and the claimed invention is that Dyrsting et al. does not expressly disclose the

(1RS,1RS)-3-(3-dimethylamino-1-hydroxy-1,2-dimethylpropylphenol salt with sugar. However, the prior art amply suggests the same as WO 00/12067 disclose the formulation of drug salts with sugars such as saccharinates and EP 0 693 475 disclose that (1RS,2RS)-3-(3-dimethylamino-1-hydroxy-1,2-dimethylpropylphenol that can be converted in a known manner to their salts. As such, it would have been well within the skill of one of ordinary skill in the art to prepare a (1RS,2RS)-3-(3-dimethylamino-1-hydroxy-1,2-dimethylpropylphenol salt with a sugar, such as saccharin, with the expectation that the same would be physiologically acceptable and provided improved organoleptic properties.

The Examiner has duly considered the Applicant's arguments but deems them unpersuasive.

The Supreme Court in *KSR International Co. v. Teleflex Inc.*, held the following:

(1) the obviousness analysis need not seek out precise teachings directed to the subject matter of the challenged claim and can take into account the inferences and creative steps that one of ordinary skill in the art would employ;

(2) the obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents;

(3) it is error to look only the problem the patentee was trying to solve-any need or problem known in the field of endeavor at the time of invention and addressed by the prior art can provide a reason for combining the elements in the manner claimed;

(4) it is error to assume that one of ordinary skill in the art in attempting to solve a problem will be led only to those elements of prior art designed to solve the same problem-

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common sense teaches that familiar items may have obvious uses beyond their primary purposes, and in many cases one of ordinary skill in the art will be able to fit the teachings of multiple patents together like pieces of a puzzle (one of ordinary skill in the art is not automaton);

(5) it is error to assume that a patent claim cannot be proved obvious merely by showing that the combination of elements was “obvious to try”. *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1396, 1397 (U.S. 2007).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Further, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

The Applicant places great emphasis on the term "certain non-alkaloid organic bases", however, the Applicant has provided no evidence that the terms excludes (1RS, 2RS)-3-(3-dimethylamine-1-hydroxy-1,2-dimethylpropyl)phenol. The Applicant's focus on the specific examples of analgesics is without merit. The types of drugs that fall within the term "certain non-alkaloid organic bases" encompass more than just codeine, meperidine, pentazocine, butorphanol or buprenorphine and include compounds having widely different structures. As such, the mere fact that codeine, meperidine, pentazocine, butorphanol or buprenorphine have

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different structures than the claimed compound is not sufficient to overcome the claimed rejection. As indicated above, one of ordinary skill in the art is not an automaton.

The Applicant's reliance on solubility to overcome the rejection is without merit. In the first instance, the relative solubility of the elected compound is not indicated. Further, it is hardly unexpected that a sacchrinate would be less soluble than the hydrochloride salt. HCl (a strong inorganic acid) is clearly more soluble than saccharine (an organic molecule) in water. As such, all other things being equal, it is not unexpected that a hydrochloride salt would be more soluble than a saccharine salt.

The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. See, e.g., *Cross Med. Prods., Inc. v. Medtronic Sofamor Danek, Inc.*, 424 F.3d 1293, 1323, 76 USPQ2d 1662, 1685 (Fed. Cir. 2005) (“One of ordinary skill in the art need not see the identical problem addressed in a prior art reference to be motivated to apply its teachings.”); *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972); *In re Dillon*, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1990), cert. denied, 500 U.S. 904 (1991). As such, the improvement of organoleptic properties provides sufficient reasoning to combine the references. The Applicant's argument as to tablets intended to be swallowed does not overcome the rejection. Even a tablet which is intended to be swallowed can come into contact with the tongue, by the tablet itself or any dissolved components due to the action of saliva or liquid used to facilitate swallowing of the tablet, or by any other action of the patient and/or administrator to intentionally or unintentionally cause the tablet contents to come in contact with the tongue, and, as such, can be

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tasted. Thus, there would be reasoning to improve organoleptic properties in a tablet that is intended to be swallowed.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Conclusion

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier number for accessing the facsimile machine is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Choi whose telephone number is (571)272-0610. Examiner maintains a compressed schedule and may be reached Monday, Tuesday, Wednesday and Thursday, 6:00 am – 4:30 pm (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Johann R. Richter, can be reached at (571)272-0646. Additionally, Technology Center 1600's Receptionist and Customer Service can be reached at (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Frank Choi
Patent Examiner
Technology Center 1600
December 24, 2008

/Johann R. Richter/
Supervisory Patent Examiner, Art Unit 1616